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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,649	04/19/2001	Alastair Murchie	22620/1222	2120

29933 7590 06/27/2003

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EXAMINER
CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
1637	21

DATE MAILED: 06/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/839,649	MURCHIE ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Acknowledgement is made for the request to establish continued prosecution application (RCE) (Paper NO. 20) filed on May 15, 2003. The request for RCE is accepted and is established with the status of the application as follows:

a. the filling date of this RCE is established as April 15, 2001;

b. claims 1-13 and 16 are pending and are considered for examination in view of the amendment.

2. This action is in response to the amendment filed on March 24, 2003 in Paper No. 17, in which claim 1 is amended. The instant pending claims 1-13, and 16 are considered for continued prosecution.

Response to arguments:

3. With reference to the rejection made under 35 USC 102(e) and 103(a), Applicants amendment is fully considered and found persuasive. The rejections are withdrawn in view of the amendment and new ground(s) of rejections.

New issues

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim 16 recites "suicide substrate" which is unclear and indefinite

what the suicide substrate refers to, that is whether it refers to a specific inhibitor region or apoptotic site or enzyme suppressor region or mutant substrate region of said target RNA.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

A. Claim 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Hansen et al. (RNA, Vol.5, pp. 93-101, 1999).

With reference to the instant claim 1, Hansen et al. teach a method for determining whether a test compound (DMA or kethoxal) binds to a target RNA, wherein Hansen et al. discloses that the method comprises (a) contacting said test compound with said target RNA and an RNA-modifying enzyme (ErmE methyltransferase) (see page 100, column 1, paragraphs 2-4) that covalently alters an existing base in said target RNA (see page 98, column 1, paragraph 1, Fig.3); (b) detecting the modification of said target RNA by said enzyme and comparing the amount of modification to that of a standard (untreated control), wherein said comparison determines whether said test compound binds to said target RNA (see page 100, column 1, paragraph 4, page 97, Fig.2, page 96, column 1, Fig.1).

With reference to claims 2-11, Hansen et al. also disclose that the method comprises ribosomal RNA target (see page 100, paragraph 2); (ii) target RNA includes a stabilizing

structure and chemical modification enhances the stability of said target RNA (see page 98, column 1, paragraph 1); (iii) RNA modifying enzyme is erythromycin resistance (ErmE) methyltransferase (see page 100, column 1, paragraphs 1-2); (iv) target RNA modification is detected by incorporation of a radio label S-adenosyl-methionine into the target RNA (see page 100, column 1, paragraph 2, page 95, table.1); and (v) the test compound is a small organic molecule (DMS or kethoxal) (see page 100, column 1, paragraph 3). Thus the disclosure of Hansen et al. meets the limitations in the instant claims.

B. Claims 1-7, 9, 11 rejected under 35 U.S.C. 102(e) as being anticipated by Schwartz et al. (USPN. 6,020,139).

Schwartz et al. teach a method for determining whether a test compound binds to a target nucleic acid, wherein Schwartz et al. disclose that the method comprises (a) contacting said test compound with the target sample (biological fluid comprising nucleic acids) comprising RNA-modifying enzyme (S-adenosylhomocystenine hydrolase, or methyl transferases) which form s-adenosyl-L-methionine (SAM) metabolite (see column 15, lines 16-65, column 16, lines 31-41) that covalently alters an existing base in the target sample (see column 15, lines 33-65, column 5, lines 64-67, column 6, lines 1-27, column 11, lines 62-67, column 12, lines 1-57); (b) detecting the modification of said target nucleic acid by said enzyme and comparing the amount of modification detected to that of a standard and identifying the binding of said test compound with said target RNA (see column 6, lines 3-40, column 5, lines 26-46). Schwartz et al. also teach that the (i) RNA target comprises ribosomal RNA (see column 14, lines 50-57); target RNA includes stabilizing methylated (chemical modification) structure (see column 32, lines 11-50); RNA-modifying enzyme comprises methyltransferase (column 15, lines 32-44); RNA

modification is detected by the incorporation of radiolabeled SAM (see column 5, lines 26-46); test compound is selected from the group consisting of peptide, protein, lipid, small molecule, nucleotides and a polyamine (see column 7, lines 1-61). Thus the disclosure of Schwartz et al. meets the limitations in the instant claims.

C. Claim 1-4, 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Glazer et al. (J Biol. Chem., Vol. 259, No.21, pp. 12964-12969, 1984).

Glazer et al. teach a method for determining a test compound (neplanocin A) binds to a target RNA, wherein Glazer et al. teach that the method comprises (a) contacting a test compound with a RNA-modifying enzyme (RNA methyltransferase) and said target RNA comprising suicide substrate (cytocidal substrate) for said enzyme (see page 12964, column 1, summary, column 2, paragraphs 1-8); (b) detecting the modification of the enzyme by said suicide substrate (decreased RNA methylation), wherein said detecting determines whether said test compound binds to said target RNA (see page 12965, column 1, paragraphs 1-5, column 2, paragraph 1-2). Thus the disclosure of Galzer et al. meets the limitations in the instant claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen et al. (RNA, Vol.5, pp. 93-101, 1999) in view of Karn et al. (USPN. 6,316,194).

Hansen et al. teach a method for determining whether a test compound (DMA or kethoxal) binds to a target RNA, wherein Hansen et al. discloses that the method comprises (a) contacting said test compound with said target RNA and an RNA-modifying enzyme (ErmE methyltranferase) (see page 100, column 1, paragraphs 2-4) that covalently alters an existing base in said target RNA (see page 98, column 1, paragraph 1, Fig.3); (b) detecting the modification of said target RNA by said enzyme and comparing the amount of modification to that of a standard (untreated control), wherein said comparison determines whether said test compound binds to said target RNA (see page 100, column 1, paragraph 4, page 97, Fig.2, page 96, column 1, Fig.1). Hansen et al. also disclose that the method comprises ribosomal RNA target (see page 100, paragraph 2); (ii) target RNA includes a stabilizing structure and chemical modification enhances the stability of said target RNA (see page 98, column 1, paragraph 1); (iii) RNA modifying enzyme is erythromycin resistance (ErmE) methyltransferase (see page 100, column 1, paragraphs 1-2); (iv) target RNA modification is detected by incorporation of a radio label S-adenosyl-methionine into the target RNA (see page 100, column 1, paragraph 2, page 95, table.1); and (v) the test compound is a small organic molecule (DMS or kethoxal) (see page

100, column 1, paragraph 3). However, Hansen et al. did not teach test compound selected from combinatorial library and high throughput assay format.

Karn et al. teach a method for determining a test compound binds to a target RNA, wherein Karn et al. disclose that the method comprises (i) incubating a test compound with target RNA and an antimicrobial molecule, measuring or detecting the change or modification of said target RNA and comparing the amount of change to that of a standard and identifying test compounds that bind to the target RNA (see column 3, lines 51-67, column 4, lines 1-26). Karn et al. also disclose that the method comprises (i) target RNA as ribosomal RNA or fragment or sub-regions of ribosome or complete RNA (see column 4, lines 36-42, column 5, lines 53-67, and column 6, lines 1-7); (ii) target RNA could be chemically modified RNA which enhances the stability of said target RNA (see column 4, lines 36-38, column 9, lines 2-66, column 10, lines 4-67); test compounds could include peptides, peptides, lipids, metal, nucleotides, nucleosides, small organic molecules, polyamines (see column 15, lines 62-67, and column 16, lines 1-11); test compounds may be derived from large libraries of synthetic or natural compounds (combinatorial library) (see column 16, lines 12-20); and the method is designed for a high-throughput screening format (see column 19, lines 30-46).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of detecting a test compound as taught by by Hansen et al. with the method of Karn et al. which is well known in the art at the time the invention was made, because Karn et al. states that 'In most biological systems, the functions of RNA is often determined by the interactions between highly conserved RNA structures. In many instances it is desirable to develop drugs that bind RNA at sites of conserved structure to act as

competitive inhibitors of the RNA function that is derived from various RNA interactions. These types of drugs have potential applications in a wide range of diseases including bacterial, viral, and fungal infections. Many antibiotics function by inhibiting protein synthesis, and it has become increasingly clear that many do so by acting at the level of ribosomal RNA" (see column 1, lines 13-21 and column 2, lines 61-63). An ordinary practitioner would have been motivated to combine the method of Hansen et al. with the addition of high-throughput assay format and use of combinatorial library as taught by Karn et al. because the addition of such limitations would improve the method for simultaneous screening of different test compounds binding to target ribosomal RNA.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
June 20, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER